A single cell bioengineering approach to elucidate mechanisms of adult stem cell self-renewal.

Journal: Integr Biol (Camb)

Publication Year: 2012

Authors: P M Gilbert, S Corbel, R Doyonnas, K Havenstrite, K E Magnusson, H M Blau

PubMed link: 22327505

Funding Grants: Regulation of Stem Cell Fate in Bioengineered Arrays of Hydrogel Microwells, Stanford CIRM Training Program

Public Summary:
The goal of regenerative medicine is to restore form and function to damaged and aging tissues. Adult stem cells, present in tissues such as skeletal muscle, comprise a reservoir of cells with a remarkable capacity to proliferate and repair tissue damage. Muscle stem cells, known as satellite cells, reside in a quiescent state in an anatomically distinct compartment, or niche, ensheathed between the membrane of the myofiber and the basal lamina. Recently, procedures for isolating satellite cells were developed and experiments testing their function upon transplantation into muscles revealed an extraordinary potential to contribute to muscle fibers and replenish the satellite cell compartment. However, these properties are rapidly lost once satellite cells are cultured. Accordingly, making the role of extrinsic factors in controlling muscle stem cell fate, in particular self-renewal, is critical. Through careful design of bioengineered culture platforms, analysis of specific proteins presented to stem cells is possible. Critical to the success of the approach is single cell analysis, as more rapidly proliferating progenitors may mask the behavior of stem cells that proliferate slowly. Bioengineering approaches provide a potent means of gaining insight into the role of extrinsic factors in the stem cell microenvironment on stem cell function and the mechanisms that control their diverse fates. Ultimately, the multidisciplinary approach presented here will lead to novel therapeutic strategies for degenerative diseases.

Scientific Abstract:
The goal of regenerative medicine is to restore form and function to damaged and aging tissues. Adult stem cells, present in tissues such as skeletal muscle, comprise a reservoir of cells with a remarkable capacity to proliferate and repair tissue damage. Muscle stem cells, known as satellite cells, reside in a quiescent state in an anatomically distinct compartment, or niche, ensheathed between the membrane of the myofiber and the basal lamina. Recently, procedures for isolating satellite cells were developed and experiments testing their function upon transplantation into muscles revealed an extraordinary potential to contribute to muscle fibers and access and replenish the satellite cell compartment. However, these properties are rapidly lost once satellite cells are plated in culture. Accordingly, elucidating the role of extrinsic factors in controlling muscle stem cell fate, in particular self-renewal, is critical. Through careful design of bioengineered culture platforms, analysis of specific proteins presented to stem cells is possible. Critical to the success of the approach is single cell analysis, as more rapidly proliferating progenitors may mask the behavior of stem cells that proliferate slowly. Bioengineering approaches provide a potent means of gaining insight into the role of extrinsic factors in the stem cell microenvironment on stem cell function and the mechanisms that control their diverse fates. Ultimately, the multidisciplinary approach presented here will lead to novel therapeutic strategies for degenerative diseases.